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Molecular electrostatic field as useful descriptor of molecular lipophilicity

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Lipophilicity is of considerable interest for the prediction of transport, adsorption and distribution properties of molecules and as such, represent an important factor in drug design [1]. According to very complex nature of lipophilicity, sophisticated and time consuming simulations are necessary for quantitative treatment. In this study the simple method for qualitative description of molecular lipophilicity based on statistical analysis of molecular electrostatic potential (MEP) and molecular electrostatic field (MEF) are proposed.

The triangulated solvent excluded surface (vertices + faces) were generated with MSMS [2] program. The additional six points for each vertices at the molecular surface were generated due to numerical calculation of molecular electrostatic field. MEP and MEF at those points were calculated using modified MOPAC 97 [3] and AM1 and PM3 model were applied. The statistical analysis and VRML graphical representation of MEP and MEF at the molecular surfaces were made by homemade programs.

The descriptors obtained with the statistical analysis of MEP and MEF show good agreement with the experimental logP values for model compounds: acids, alcohols, amines and hydrocarbons. The VRML graphical representation of MEF is very useful for localisation of molecular lipophilicity.

1. Q., Du, G.A., Arteca and Mezey, P.G. Heuristic lipophilicity potential for computer-aided rational drug design. *Journal of Computer-Aided Molecular Design*, 11 (1997) 503-515.

2. M., Sanner, M.F., Spehner, J.-C., and Olson, A.J. Reduced surface: an efficient way to compute molecular surfaces. *Biopolymers*, 38 (1996) 305-320.

3. MOPAC 97 (c) Fujitsu.